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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,543	04/09/2002	Satoru Yokomizo	12218/3	1045

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KENYON & KENYON
 1500 K STREET NW
 SUITE 700
 WASHINGTON, DC 20005

EXAMINER

AKHAVAN, RAMIN

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/019,543

Applicant(s)

YOKOMIZO ET AL.

Examiner

Ramin (Ray) Akhavan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 5, 7-24 and 26-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 9, 12 and 13 is/are allowed.
- 6) ☒ Claim(s) 1-3, 5, 7, 8, 10, 11, 14-24 and 26-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a response, filed 05/06/05, canceling claims 6 and 25, adding new claims 26-30 and amending claims 1, 9, 10, 12, 13, 15, 16 and 18. Claims 1-3, 5, 7-24 and 26-30 are under consideration in this action. All objections/rejections not repeated herein are hereby withdrawn.

Where applicable, a response to Applicant's arguments will be set forth immediately following the body of any objections/rejections repeated herein. As any new grounds of rejection are necessitated by material changes to the claims, **this action is made FINAL**.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

- 1. Claims 11, 18-23, 26-27 and 29-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

This is a new ground of rejection necessitated by amendment to the claims.

Claim 11 recites that the promoter and terminator are isolated from *Candida maltosa*, which species of yeast lacks sufficient antecedent support. Claim 11 depends from claim 7 which recites that the promoter and terminator function in "the yeast". Claim 7 depends from claim 1 which recites *the yeast* cell as selected from various genera of yeast, none of which include *Candida*. Thus, the limitation *Candida maltosa* lacks antecedent support.

Independent claim 18 recites the phrase “said gene expresses its function in a yeast”, which confers ambiguity with respect the claims’ metes and bounds. Particularly, it is unclear what is being claimed with respect to the limitation “expresses its function”. A gene encodes or expresses a protein. Thus, where a protein is expressed, whether functional or not, the claim limitation would be met; presumably, this is not the embodiment that is intended.

Applicant appears to be interpreting the limitation “expresses its function” to mean expressing a functional protein. (Remarks, p. 8, paragraph discussing claim 18; indicating that exogenous genes “express their functions”). In other words, where a modification is made to a CTG codon, the PSA protein functionality is unaltered. However, as written, the claim would not necessarily be interpreted as such, thereby making the claim’s metes and bounds unclear. The claim would be clear and definite, if for example it recited the phrase “expresses a functional polyester synthesis-associated enzyme”, thus indicating that a functional protein is expressed, notwithstanding the requisite codon alteration.

In addition, claim 29 recites the limitation “the cassette comprising two polyester synthesis-associated enzyme genes”, which lacks sufficient antecedent support in base claim 1. Claim 1 is directed to an expression cassette with “a...gene”. However, it would be remedial to clarify the claim’s boundaries by including language such as “the cassette further comprises a second polyester synthesis-associated enzyme gene”.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 28 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Fukui et al. (US 5,981,257; the '257 patent; reference already of record).

This rejection is of record as applied to claims that previously were directed to the transformant as selected from the genus *Candida*. It is applied to the new claims 28 and 29, which as a result of amendments to the claims, are directed to transformants selected from the genus *Candida*. The claims, as amended, are directed to a transformant that comprises a PSA gene, a promoter and a terminator, where the transformant is delimited to several genera of yeast including *Candida*.

The '257 patent teaches cells transformed with nucleic acids that comprise a polyester synthase gene wherein the polyester polymer formed comprises 3HB-co-3HH. (e.g. col. 1, ll. 25-55; col. 11, Table 3). Furthermore, the PHA gene or the enoyl-CoA hydratase gene that is obtained from the bacterium - *Aeromonas caviae*. (e.g., col. 3, l. 32; col. 7, ll. 20-66). The '257 patent explicitly teaches that the host organism, transformed with an expression vector, can be yeast, more particularly *Candida*. (e.g., col. 4, l. 26). Furthermore, if yeast are to be used as the host organisms, the '257 patent teaches that appropriate expression vectors, such as Yep13 or Ycp50 can be used to provide appropriate promoters/terminators, whereby an expression construct comprising a gene would necessarily comprise a promoter and terminator functional in the host yeast cell. (e.g. col. 4, l. 47). Therefore, the '257 patent anticipates the rejected claims.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

- 3. Claims 1-3, 5, 7-8, 10, 14-15, 17, 24 and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over of Fukui et al. (US 5,981,257), further in view of Park et al. (J. Biol. Chem. 1997; 272(11): 6876-81).**

This rejection is of record and repeated herein in salient part. It is a new rejection insofar as being applied to new claims 28-29. A response to Applicant's arguments is set forth immediately following the body of this rejection. (Infra, Response to Arguments). The claims are directed to a transformant that comprises a PSA gene, a promoter and a terminator, where the transformant is delimited to several genera of yeast including *Yarrowia*.

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Additional limitations further particularize the species of yeast to *Yarrowia lipolytica* and further particularize the promoter in the expression construct to a promoter of the XPR2 gene isolated from *Y. lipolytica*.

The '257 patent teaches cells transformed with nucleic acids that comprise a polyester synthase gene wherein the polyester polymer formed comprises 3HB-co-3HH. (e.g. col. 1, ll. 25-55; col. 11, Table 3). Furthermore, the PHA gene or the enoyl-CoA hydratase gene that is obtained from *Aeromonas caviae*. (e.g., col. 3, l. 32; col. 7, ll. 20-66; claims 28-29). The '257 patent explicitly teaches that the host organism, transformed with an expression vector, can be yeast, more particularly *Candida*. (e.g., col. 4, l. 26).

Furthermore, if yeast are to be used as the host organisms, the '257 patent teaches that appropriate expression vectors, such as Yep13 or Ycp50 can be used to provide appropriate promoters/terminators, whereby an expression construct comprising a gene would necessarily comprise a promoter and terminator functional in the host yeast cell. (e.g. col. 4, l. 47; claim 28).

The '257 patent teaches that PHA genes from *A. caviae* will operate in the same yeast cells as Leaf et al. (i.e., *S. cerevisiae*). In addition, as stated previously, the '257 patent teaches that additional yeast, such as *Candida*, can be transformed with the PHA gene from *A. caviae*. (e.g., col. 4, l. 26). Both Leaf et al. and the '257 patent teach transformed yeast cells expressing PHA genes in order to harvest polyesters therefrom. Indeed, Applicant's own disclosure teaches that the yeast cells used are not particularly important. (e.g., Specification, p. 6, ll. 30-33). Furthermore, the '257 patent teaches that the host cells used are not particularly limiting. (e.g., col. 4, ll. 16-20).

The '257 patent does not explicitly teach that *Y. lipolytica* can be the transformed yeast cell, but as stated previously, the reference explicitly states that the type of cell is not particularly limiting (e.g., col. 4, ll. 22-28), an assertion that is also disclosed in instant specification. (e.g., p. 6, bottom). In addition, the '257 patent does not teach that the promoter on the expression construct can be from the XPR2 gene isolated from *Y. lipolytica*. The '257 patent is drawn to the art of utilizing yeast cells, such as *S. cerevisiae* or *Candida* in expression of heterologous proteins (e.g., PHA enzymes). Substituting various yeast host cells is not considered the inventive step for the instant invention, as Applicant clearly concedes. (Specification, p. 6, ll. 30-33).

Park et al. teach transformed cells wherein expression constructs containing XPR2 promoters/terminators are used in a system for expression of heterologous proteins in *Y. lipolytica*. (e.g., Abstract; pages 6876-81). More particularly, *Y. lipolytica* is transformed with expression constructs, with said XPR2 gene promoter/terminators, in order to express a heterologous α -Amylase enzyme. Therefore, the issue can be framed as whether one of skill would recognize that various yeast cells, particularly *Y. lipolytica*, could be utilized in expressing heterologous proteins/enzymes, such as PHA. Park et al. teach that *Y. lipolytica* provides certain advantages of *S. cerevisiae*, in a process of using transformed cells to express a heterologous protein. (e.g., p. 6876, col. 1, ¶ 1, bridging to col. 2, ¶¶ 1-2). Furthermore, Park et al. teach that it is well known in the art that the XPR2 gene comprises a strong promoter that has been used to express heterologous proteins in *Y. lipolytica*. (e.g., p. 6876, col. 2, ¶ 3).

Therefore it would have been obvious to substitute the transformed cells as taught by the '257 patent, with the transformed *Y. lipolytica* cells comprising the XPR2 promoter/terminator

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constructs as taught by Park et al. in order to obtain the benefit of a strong and well tested yeast cell system necessary to express a heterologous protein (e.g., PHA enzyme). One would have been motivated to make such a substitution to expand the range of yeast cell cultures that could be used to produce the heterologous proteins such as the PHA enzymes, as well as to obtain the benefits taught by Park et al. compared to *S. cerevisiae* as the culture cell. Given the level of skill at the time of invention, one of ordinary skill in the art would have had a reasonable expectation of success in substituting the transformed *S. cerevisiae* cells of the '257 patent with the *Y. lipolytica* transformed cells as taught by Park et al.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicants assert that neither the '257 patent or Park teach or suggest the claimed transformant cell to be one from any of the genera as recited in claim 1. (e.g., Remarks, p. 9, middle).

Applicant's attention is respectfully directed to the rejection of record repeated herein above, which clearly states that Park explicitly teaches *Yarrowia lipolytica*, which is a genus of yeast that is recited in claim 1. (Park, pages 6876-81; each page reciting *Yarrowia lipolytica*). Furthermore, as Applicant well points out, selecting the type of yeast host cell is not particularly important to the invention. (Specification, p. 6, ll. 30-33). Applicant does not present any other arguments. In view of the foregoing, the rejection is maintained.

Allowable Subject Matter

Claims 9, 12 and 13 are allowed..

Conclusion

Claims 9, 12 and 13 are allowed. Claims 1-3, 5, 7-8, 10-11, 14-24 and 26-30 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached between 8:30-5:00, Monday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD, can be reached on 571-272-0781. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully submitted,

Ray Akhavan/AU 1636


DAVID GUZO
PRIMARY EXAMINER